

# BRITISH MEDICAL JOURNAL

LONDON SATURDAY 18 JULY 1964

## Pointers

**Human Experimentation:** Text of W.M.A. Code (p. 177). Medical Research Council statement on investigations on human subjects (p. 178). Leader on this page.

**Royal College of Psychiatrists:** Leader at p. 137.

**Haemolytic Disease of Newborn:** Dr. W. Walker and colleagues assess prognostic significance of bilirubin, protein, and haemoglobin in amniotic fluid. "Examination of liquor . . . is of great practical value" (p. 141). Mr. J. G. Robertson discusses use of a diazo test for indirect bilirubin (p. 147). Leader at page 136.

**Eczema of Hands:** Dr. F. Ray Bettley reviews aetiology, treatment, and prognosis of 106 cases, with special reference to role of "causative factors" (p. 151).

**Rubella Syndrome:** Dr. J. A. Dudgeon and colleagues describe serological findings in 31 children with congenital defects after maternal rubella. Neutralizing antibody was raised (p. 155). Dr. H. E. M. Kay and colleagues report isolation of rubella virus from 23-week human embryo (p. 166).

**Treatment of Neurosis:** After a 5-year follow-up of neurotic out-patients Dr. R. Giel and colleagues conclude that psychiatric treatment failed to affect final outcome (p. 160).

**Coeliac Disease:** Dr. W. M. McCrae and Dr. Elizabeth Sweet find that active disease is always accompanied by x-ray changes and advocate x-ray examination as screening test (p. 163).

**Sonne Dysentery:** Dr. C. E. D. Taylor and Mr. G. V. Heimer describe rapid fluorescent-antibody diagnostic test (p. 165).

**Rabies:** Human case in England (p. 167).

**Alpha-methyl dopa:** Parkinsonism (p. 168).

**Obstetrics in G.P.:** Mr. J. Stallworthy discusses "Home or Hospital?" (p. 169).

**To-day's Drugs:** Chlormethiazole (p. 171).

**Ventriculostomy Reservoir:** Described by Mr. P. P. Rickham (p. 173).

**M.R.C. Annual Report:** Survey of current research (p. 180).

**Jane Austen:** Sir Zachary Cope on her last illness (p. 182). Leader at p. 140.

**Pertinax** in "Without Prejudice" (p. 184).

**Emigration of Doctors:** Letters from Dr. J. Seale, Dr. R. Hale-White, and others (p. 185).

**Sulphonylurea Drugs:** In pregnancy (p. 187).

**Community Mental Services:** Discussed in Parliament (p. 198).

**G.M.S. Committee:** First meeting of new committee (*Supplement*, p. 31).

**Conference of L.M.C.s:** Concluded (*Supplement*, p. 33).

## Ethics of Human Experimentation

Two important contributions on the ethics of human experimentation are published in the middle pages of this week's *B.M.J.* One is a statement by the Medical Research Council in its Annual Report to Parliament published this week.<sup>1</sup> The other is a much revised version by the World Medical Association of its draft code on the ethics of human experimentation which was published in this Journal two years ago.<sup>2</sup> This complex matter has been discussed several times in these columns,<sup>3 4 5 6 7</sup> and two papers dealing with specific problems of the ethics of experiments on human beings were published this year, one on the ethics of experiments in paediatrics<sup>8</sup> and the other on the ethical problems involved in the grafting of organs,<sup>9</sup> the first by Professor R. G. Mitchell and the other by Professor M. F. A. Woodruff. Many other communications on the ethics of human experimentation have been read and published, and the matter has naturally enough aroused great interest and justifiable concern in the public mind. Familiarity with research procedures has apparently made it easy for medical men to forget at times that their patients—or volunteers—are human beings and not experimental animals. This must be a matter of grave concern to every medical man whether he practises among the general public or makes his investigations in the laboratory. We have as a profession departed a long way from the simple principles laid down by the father of experimental medicine, Claude Bernard. It will suffice to recall here two of his dicta: "So, among the experiments that may be tried on man, those that can only harm are forbidden; those that are innocent are permissible; and those that may do good are obligatory." And he also wrote this: "The principle of medical morality consists, then, in never performing on man an experiment which can be harmful to him in any degree whatsoever though the results may be of great interest to science—that is of benefit to save the health of others."

During the last war a certain number of German doctors conducted in concentration camps experiments on the inmates that shocked the conscience of the world when the nature and extent of these were revealed at the Nuremberg Trials. This led the Tribunal to draw up a ten-point code to serve as a guide for those carrying out research on human beings.<sup>10</sup> This Nuremberg Code was to all intents and purposes adopted by the United States Public Health Service,<sup>11</sup> and the American Medical Association also gave some general guidance, as has recently the British Medical Association.<sup>12</sup> Doubt has been expressed whether a code of ethics on human experimentation is necessary or even desirable, and those holding this view believe more in the efficacy of such matters as the doctor's conscience, and such general statements that you should not do to others things you would not have done either to yourself or to members of your family.

On the whole there has been a tendency, especially on the part of those concerned with experimental work, to avoid stating in clear terms

what are the desirable limits within which the medical research worker should remain. This resistance is an interesting phenomenon, especially in view of Medicine's long traditional adherence to such codes as the Hippocratic Oath and the importance attached by doctors all over the world to codes governing their behaviour in relation to their patients. The Medical Research Council in 1953 drew up a general statement to indicate its "attitude towards the considerations involved in carrying out investigations on patients." This was a most important step, and the memorandum, then circulated to members of the Council's staff and to others, showed the Council's awareness of the hazards in this field of investigation and its anxiety to do something to draw workers' attention to them. The Council then expressed the view that in "clinical research it is impossible to frame a code of general advice that would adequately cover the ever changing circumstances which arise." But the very much fuller statement now issued by the M.R.C. in its current Annual Report shows that it has found it necessary to expand considerably its memorandum of 1953 into a statement which broken up by numbered paragraphs will be getting near to a code of ethics of human experimentation bearing some imprint of the draft code of the W.M.A. published two years ago.

The revised code of the W.M.A. published in this week's *B.M.J.* suffers partly because it is a translation from a revision in French of the original code, and also because it is less concise and omits certain clauses that we believe would have strengthened it. What so many fail to grasp is that a code can be no more than a guide in the form of signposts pointing to desirable directions. After all, human conduct has been governed for centuries by the famous ten-point code of Moses. And although the Commandment "Thou Shalt Not Kill" was explicit, human societies, accepting this, have nevertheless shown by their constitutional actions that they accept it as a guide and not as a categorical imperative.

If the medical profession in the U.S.A. had accepted the W.M.A. code as a guide to its action, the incident in Boston to which attention has recently been drawn by a letter to the *New England Journal of Medicine* of 7 May this year,<sup>13</sup> and a leading article on it, might not have occurred. In the issue of that journal of 2 April<sup>14</sup> an article was published under the title of "Effect of thymectomy on skin-homograft survival in children." "This is a report of data obtained from children, beyond the neonatal stage, undergoing major corrective heart surgery, in which the thymus is frequently dissected and partially removed for aortic-arch exposure. When desired, a complete thymectomy could be accomplished without increasing the hazards of surgery. Thus, an opportunity for the study of skin-homograft survival in patients having a carefully performed thymectomy was available for the first time." Of 18 children between the ages of 3½ months to 18 years of age that were operated on for congenital heart disease for the experimental investigation 11 had a total

thymectomy and seven, serving as controls, "had only a biopsy of the thymus." At the end of each operation a full-thickness skin homograft was sutured in place on the chest wall. The fate of the grafts was observed and other data were obtained. The authors note that animal experiments had shown the disappearance of alpha globulin after thymectomy in adult dogs, and intend to repeat analyses in the thymectomized children to define whether a similar change may occur in them some months later. Dr. Byron H. Waksman in his letter to the *New England Journal of Medicine* of 7 May calls in question the ethics of this investigation, because "it was carried out as a purely experimental measure in subjects not having a disease to which this procedure is relevant." The leading article in the same issue shows the disquiet that must be felt by many about an experiment which "involves children who cannot speak for themselves and for whom not even the parent can honestly speak unless the particular procedure is obviously justified in each case." The leader recommends "not only that a reasonable, generally acceptable code of ethics be put into practice, but that the individual investigator develop a sense of values that will lead him almost instinctively to know how far he can go with propriety in a given set of circumstances." And the leader writer goes on to state: "A blind adherence to an inflexible code may be unrealistic, but an honestly cultivated sense of ethics should point to the right course."

We have given this particular example in some detail because it is recent, and not because it represents any new lapse from "a cultivated sense of ethics." Similar examples could be quoted from British literature. The reference to an inflexible code shows the prevalent anxiety among investigators that a guide drawn up by doctors for themselves will be looked upon as having the force of law. We suggest that their real fear is of interference with the freedom of the investigator to decide for himself what is ethical or not without the help of a code. The medical profession has departed far enough from elementary principles of human behaviour and from such general guidance as was offered by Claude Bernard and others to show that pious general statements are of little, if any, value. For this reason we welcome the revised code of the World Medical Association, while regretting that its revision has to some extent weakened it. We welcome, too, the more detailed guidance now given by the Medical Research Council, which in many respects offers a more realistic and sounder guide to the research worker who is enlarging the field of human knowledge by investigating human beings.

## Amniocentesis

Haemolytic disease of the newborn, though relatively rare, now accounts for about 4% of the perinatal deaths in the United Kingdom,<sup>1</sup> and while replacement transfusion has decreased the incidence of the most dreaded manifestation, kernicterus, the obstetrician is still faced with great difficulty in the management of the Rhesus-sensitized patient, particularly when the father is heterozygous. The aim of treatment, as Dr. W. Walker and his colleagues point out at p. 141 of this week's *Journal*, is to prevent stillbirth. Even with a complete history of the patient and her past pregnancies the decision to interfere and induce premature labour is often empirical, as clinical judgment—vital though this is—will not

<sup>1</sup> Report of the Medical Research Council for the Year 1962-63. H.M. Stationery Office, Cmnd. 2382. 16s. 6d.

<sup>2</sup> *Brit. med. J.*, 1962, 2, 1119.

<sup>3</sup> *Ibid.*, 1955, 1, 215.

<sup>4</sup> *Ibid.*, 1955, 1, 526.

<sup>5</sup> *Ibid.*, 1956, 2, 762.

<sup>6</sup> *Ibid.*, 1963, 1, 1043.

<sup>7</sup> *Ibid.*, 1963, 2, 1.

<sup>8</sup> *Ibid.*, 1964, 1, 721.

<sup>9</sup> *Ibid.*, 1964, 1, 1457.

<sup>10</sup> See Clegg, H., *World Medical Journal*, March 1960, p. 77. (See also

Bradford Hill, Sir Austin, *Brit. med. J.*, 1963, 1, 1043.)

<sup>11</sup> *Ibid.*, Henry K. Beecher, p. 79.

<sup>12</sup> *Brit. med. J. Suppl.*, 1963, 2, 57.

<sup>13</sup> *New Engl. J. Med.*, 1964, 270, 1019.

<sup>14</sup> Zollinger, et al., *ibid.*, 1964, 270, 707.